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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/416,384	10/12/99	BLUMENFELD M	GENSET.045AU

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EXAMINER	
FREDMAN, J	

ART UNIT	PAPER NUMBER
1655	13

DATE MAILED: 04/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/416,384	Applicant(s) Blumenfeld et al
	Examiner Jeffrey Fredman	Group Art Unit 1655

☒ Responsive to communication(s) filed on *Mar 13, 2001*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-59, 62, 68, and 70-73* is/are pending in the application.

Of the above, claim(s) *1-44 and 47-57* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *45, 46, 58, 59, 62, 68, and 70-73* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Specification

1. The substitute pages were acceptable.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 45, 46, 58, 59, 62, 68 and 70-73 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The current claims are drawn to a genus of polypeptides termed G713 proteins in the specification, antibodies against the G713 proteins, and a method of use of the antibody for detection of the G713 protein.

Following the requirements of the Utility Guidelines (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for Utility.), the first inquiry is whether a credible utility is cited in the specification for use of the proteins. The only cited utilities identified by the examiner are to detect the protein itself, to make antibodies and to screen drugs. These utilities are credible.

Upon identification of credible utilities, the next issue is whether there are any well established utilities for the protein. No well established utilities for this specific G713 protein are identified in either the specification or in the cited prior art.

Given the absence of a well established utility, the final issue is whether substantial and specific utilities are disclosed in the specification. Here, no substantial utilities which are specific to this protein are identified. As noted in the utility guidelines, methods of treating unspecified diseases, basic research on a product to identify properties, intermediate products which themselves lack substantial utility are all insubstantial utilities. No substantial utility is identified for the specific G713 proteins of the specification, with only speculative utilities that lack any basis provided. Further, none of the recited utilities in the specification are specific to the G713 protein. None rely on any unique feature of this protein.

Finally, with regard to the utility analysis, the current situation directly tracks Example 4 of the utility guidelines, where a protein of entirely unknown function was characterized as lacking utility.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 59 and 71-73 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The current claims are drawn to a genus of any G713 proteins which comprise any six amino acids selected within positions 203 to 458 of SEQ ID NO: 5 and antibodies thereto and methods of use. This large genus is represented in the specification by only SEQ ID NO: 5. Thus, applicant has express possession of only one amino acid species in a genus which comprises hundreds of millions of different possibilities. The written description guidelines note regarding such genus/species situations that "Satisfactory disclosure of a ``representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.) Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided.

Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding

> for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic acid and amino acid sequence of the disclosed SEQ ID Nos are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of any nucleic acids acids modified by addition, insertion, deletion, substitution or inversion with the disclosed SEQ ID Nos. No correlative function which permits any determination of whether the same protein is made is disclosed in the specification.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. The rejection of claim 45 under 35 U.S.C. 102(b) as being anticipated by Wimmer et al is withdrawn in view of the amendment.

8. The rejection of claims 45 and 69 under 35 U.S.C. 102(a) as being anticipated by Bartsch et al is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 102/103

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 45, 46, 58, 59, 62, 68 and 70-73 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hanson et al (J. Exp. Med. (1992) 176:565-573)..

Hanson teaches a protein of 50 kD which is found in neuronal cells as well as antibodies which immunoreact with this protein (abstract). Hanson further teaches an assay in which the antibodies are incubated with a sample in order to determine whether the protein is present or absent (abstract).

Regarding 102/103 rejections, the MPEP 2112 states

" A REJECTION UNDER 35 U.S.C. 102 / 103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the Examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102 / 103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best,195 USPQ 430, 433 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, 35 U.S.C. 102 / 103 rejection is appropriate for these types of claims as well as for composition claims.

EXAMINER MUST PROVIDE RATIONALE OR EVIDENCE TENDING TO SHOW INHERENCY

> "In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." Ex parte Levy, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original) (Applicant's invention was directed to a biaxially oriented, flexible dilation catheter balloon (a tube which expands upon inflation) used, for example, in clearing the blood vessels of heart patients). The examiner applied a U.S. patent to Schjeldahl which disclosed injection molding a tubular preform and then injecting air into the preform to expand it against a mold (blow molding). The reference did not directly state that the end product balloon was biaxially oriented . It did disclose that the balloon was "formed from a thin flexible inelastic, high tensile strength, biaxially oriented synthetic plastic material." Id. at 1462 (emphasis in original). The examiner argued that Schjeldahl's balloon was inherently biaxially oriented. The Board reversed on the basis that the examiner did not provide objective evidence or cogent technical reasoning to support the conclusion of inherency.).
>
> ONCE A REFERENCE TEACHING PRODUCT APPEARING TO BE SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION AND THE EXAMINER PRESENTS EVIDENCE OR REASONING TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE
>
> "The PTO can require an applicant to prove that the prior art products do not necessarily possess the characteristics of his [or her] claimed product. ***Whether the rejection is based on `inherency' under 35 U.S.C. 102, on `prima facie obviousness' under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the same." The burden of proof is similar to that required with respect to product - by - process claims. In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980) (quoting In re Brown,173 USPQ 685, 688 (CCPA 1972))."

Here, Hanson teaches all of the characteristics of the claimed protein disclosed in the specification, with the sole exception of the sequence, which is an inherent property of the protein. The claimed protein has only two identifiable characteristics, it's predicted molecular

weight of approximately 50 kd, and it's location in neuronal type cells. Hanson meets both of these limitations, so that the Hanson prior art is silent regarding the inherent characteristic of protein sequence. Since the examiner has shown a reference product that, based upon the only characteristics available is identical to the protein claimed, the burden shifts to the applicant to show an unobvious difference.

Response to Arguments

12. Applicant's arguments filed March 13, 2001 have been fully considered but they are not persuasive.

The instant application does not disclose the biological role of the G713 protein or its significance. Applicant argues that the G713 protein has utility on three grounds: a small degree of homology to the TED protein, the presence of CAG repeat elements, and genomic location at 13q31-33.

These utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the G713 protein of the instant invention. The disclosed protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins, particularly the TED protein. This homology is relatively limited and provides no evidence that the G713 protein will have any shared characteristics with the TED protein. After further research, a specific and substantial credible utility might be found for the claimed isolated

compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the G713 of the instant application was, as of the filing date, similiar to the TED protein, was related to a mental disorder based upon the CAG repeats, or related to schizophrenia based solely upon chromosomal location. Until some actual and specific significance can be

attributed to the protein identified in the specification, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The DNA of the instant invention and the protein encoded thereby are compounds which share some structural similarity to TED proteins based on sequence similarity. To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability.

With regard to diagnosis of disease such as schizophrenia, in order for a G713 polypeptide to be useful, as asserted, for diagnosis of a disease such as schizophrenia, there must be a well-established or disclosed correlation or relationship between the claimed G713 polypeptide and a disease or disorder. The presence of a G713 polypeptide in a chromosomal location that is associated with schizophrenia is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression or function of the claimed G713 polypeptide and schizophrenia. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed G713 polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed G713 polypeptide is either present

only in disease tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e. overexpression) or lower levels in diseased tissue compared to normal tissue (underexpression) or differentially expressed in some other way. Evidence of a differential expression might serve as a basis for use of the claimed G713 polypeptide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the claimed G713 protein and any disease or disorder and the lack of any correlation between the claimed G713 protein with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. The disclosure does not present a substantial utility that would support the requirement of 35 U.S.C. §101.

The question at issue is whether or not the broad general assertion that the claimed proteins might be used for *some* diagnostic application in the absence of a disclosure of *which* diagnostic application would be considered to be an assertion of a specific, substantial, and credible utility. For reasons set forth above the disclosure satisfies none of the three criteria and lacks utility. *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound

in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.')

The only claim remaining rejected under written description is claim 59, 71-73, which is drawn to 6 amino acid fragments and antibodies thereto. Description of the two full length sequences does not provide descriptive support for any polypeptide which comprises these 6 amino acid fragments.

With regard to the 102/103 rejection, Applicant has identified additional art which might properly be cited against the claims as teaching proteins which fall within the scope of the claims. Applicant argues that no prima facie showing of identity has been made. This is incorrect. Every available feature was properly matched. That is, the size of the protein is identical to that of the claimed protein, and the cell source is identical as well. The examiner cannot create a closer match because Applicant has not provided any other characteristics of the protein for comparison. Thus, a prima facie case has been made with the best available evidence. It is Applicant's burden to rebut this prima facie case with evidence, since the Patent Office lacks laboratories or other facilities in which to make these determinations. The Cimato reference cited by Applicant is deemed cumulative to the current rejection.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeff Fredman, Ph.D. whose telephone number is (703) 308-6568.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Group 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Jeffrey Fredman
Primary Patent Examiner
Art Unit 1655

April 3, 2001